



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|                                     |   |                                 |
|-------------------------------------|---|---------------------------------|
| In the Application of Goddard et al | ) | Examiner: Nancy Vogel           |
|                                     | ) |                                 |
| Serial No. 10/677,471               | ) | Group Art Unit: 1636            |
|                                     | ) |                                 |
| Filed: October 2, 2003              | ) | Confirmation No. 1021           |
|                                     | ) |                                 |
| Title: SECRETED AND                 | ) | Attorney's Docket No. 10466/484 |
| TRANSMEMBRANE                       | ) |                                 |
| POLYPEPTIDES AND NUCLEIC            | ) |                                 |
| ACIDS ENCODING THE SAME             | ) |                                 |

DECLARATION OF AUDREY GODDARD, Ph.D., PAUL J. GODOWSKI, Ph.D.,  
J. CHRISTOPHER GRIMALDI, AUSTIN L. GURNEY, Ph.D., DANIEL TUMAS,  
Ph.D. AND WILLIAM I. WOOD, Ph.D. UNDER 37 CFR § 1.131

**MAIL STOP AMENDMENT**

The Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

We, Audrey Goddard, Ph.D., Paul J. Godowski, Ph.D., J. Christopher Grimaldi, Austin Gurney, Ph.D., Daniel Tumas, Ph.D. and William I. Wood, Ph.D. declare and say as follows:

1. We are the inventors of the above-identified application.
2. At the time the present invention was made, one of the inventors, Daniel Tumas, Ph.D., was responsible for overseeing the testing of novel polypeptides, including the polypeptide PRO361, in an assay of inhibitory activity in the mixed lymphocyte relation (MLR) (Assay #67, Example 34). This assay is used to find agents that are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.
3. The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12, edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO<sub>2</sub>) and then washed and resuspended to 3x10<sup>6</sup> cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50:1 of irradiated stimulator cells, and

50:1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO<sub>2</sub> for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to 1x10<sup>7</sup> cells/ml of assay media. The assay is then conducted as described above.

Any decrease below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein. The results are indicative of the utility of the PRO polypeptides

in therapeutic applications where suppression of an immune response is beneficial.

4. Copies of pages from an internal database showing the positive results for the PRO361 polypeptide (SEQ ID NO: 83), identified by Pin number PIN996-1, in Assay #67 are attached to this declaration (with dates redacted) as Exhibit A. These experiments were performed and the results were obtained in the United States prior to August, 1999.

5. Exhibit A clearly shows that the polypeptide designated PRO361 was tested, and its ability to inhibit the mixed leukocyte reaction was determined prior to August, 1999.

6. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

A. Goddard  
Audrey Goddard, Ph.D.

1/12/08  
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Paul J. Godowski, Ph.D.

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J. Christopher Grimaldi

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Paul J. Godowski, Ph.D.

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12/19/07  
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4. Copies of pages from an internal database showing the positive results for the PRO361 polypeptide (SEQ ID NO: 83), identified by Pin number PIN996-1, in Assay #67 are attached to this declaration (with dates redacted) as Exhibit A. These experiments were performed and the results were obtained in the United States prior to August, 1999.

5. Exhibit A clearly shows that the polypeptide designated PRO361 was tested, and its ability to inhibit the mixed leukocyte reaction was determined prior to August, 1999.

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Paul J. Godowski, Ph.D.

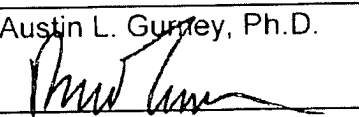
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Austin L. Gurney, Ph.D.

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Daniel Tumas, Ph.D.

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February 14, 2000  
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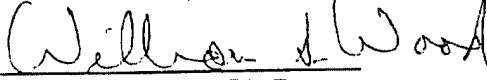
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William I. Wood, Ph.D.

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12/14/17



## **EXHIBIT A**



GenenGenes

Quick search:  Enter search terms

Quick search:  Enter ID number

SEARCH

REQUEST SYSTEMS

ANALYSIS TOOLS

RESOURCES

HISTORICAL SPDI RECORD

Assay Viewer

SPDI Assays

ASY57 Rod Photoreceptor Cell cAMP Synergy(2) Da  
ASY58 Rat DRG Neuronal Survival Inhibition Ass  
ASY59 Ventralization of Xenopus Embryo by DNA  
ASY60 Benzidine Staining of Xenopus Embryo by  
ASY61 Benzidine Staining of Xenopus Embryo by  
ASY62 Benzidine Staining of Xenopus Embryo by  
ASY63 Monoclonal: stem cell proliferation  
ASY64 Monoclonal: stem cell proliferation  
ASY65 HUVEC Survival in Absence of Serum  
ASY66 Inhibition of Apoptosis Induction  
ASY67 HUVEC Survival

Find Lots

All PIN  
All DNA

Show Lots for:

LOT:

Number:

Pin:

Include UNQ Related Lots

Look for Search

PIN996-1

Remove

☐ All Positive ☐ Verified Positives ☐ Pending

DATE Complete From

ASSAY RESULT LIST

ASY  
ASY102  
ASY103  
ASY104  
ASY105

PLB/CD/DNA  
PLB1201  
PLB1202  
PLB1203  
PLB1204

LOT  
LOT1126  
LOT1127  
LOT1128  
LOT1129

LOT Name  
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PROTEIN NAMES  
Human MANSC1 195  
Human MANSC1 195  
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Comment

DATE DATE

DATE Feedback | Selected  
GenenGenes is maintained by GenenGenes